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EXAMINER	
HALVORSON, MARK	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/506,763	VOLLMERS ET AL.	
	Examiner	Art Unit	
	Mark Halvorson	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 December 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *79 and 95-124* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *102 and 103* is/are allowed.

6)☒ Claim(s) *79, 95-101 and 104-124* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 79 and 95-124 are pending and under examination.

35 USC § 112 1st paragraph rejection maintained

The rejection of claims 79, 95-101 and 103-105 and new claims 106-124 for failing to comply with the written description requirement is maintained.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The claims are drawn to a purified antibody that specifically binds to an epitope of an antigen expressed by at least one of HT-29, CACO-2, COLO-320 or COLO-678 cells, wherein CM-1 antibody specifically binds to said epitope of the antigen expressed by at least one of HT-29, CACO-2, COLO-320 or COLO-678 cells. The dependent claims limit the sequence disparity between the claimed antibody and the antibody comprising SEQ ID NOs: 1 and 3. Thus, the claims are drawn to a genus of purified antibodies that specifically binds to an epitope of an antigen expressed by at least one of HT-29, CACO-2, COLO-320 or COLO-678 cells, wherein CM-1 antibody specifically binds to said epitope of the antigen expressed by at least one of HT-29, CACO-2, COLO-320 or COLO-678 cells.

The specification discloses an IgM antibody, CM-1, that induces apoptosis of a neoplastic cell but does not induce apoptosis of a non-neoplastic cell wherein the antibody specifically binds to at least one of HT-29, CACO-2, COLO-320, COLO-206F, or COLO-678 cells, the antibody comprising a heavy chain variable region consisting of the amino acid sequence of SEQ ID NO: 1, and a light chain variable region consisting of SEQ ID NO:3. Neither the specific epitope nor the specific antigen bound by the claimed antibody is disclosed. Thus, as in In re Alonso, (Fed Cir 2008) the specification

teaches nothing about the structure , epitope characterization, binding affinity specificity or pharmacologic properties common to the large genus of antibodies encompassed by the present claims.

The Federal Circuit addressed the application of the written description requirement to DNA-related inventions in University of California v. Eli Lilly and Co., 119 F.3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997). The court stated that "[a] written description of an invention involving a chemical genus, like a description of a chemical species, requires a precise definition, such as by structure, formula, [or] chemical name, of the claimed subject matter sufficient to distinguish it from other materials." Id. At 1567, 43 USPQ2d at 1405. The court concluded that "naming a type of material generally known to exist, in the absence of knowledge as to what that material consists of, is not a description of that material." Id.

The Federal Circuit has recently clarified that a molecule can be adequately described without disclosing its complete structure. See Enzo Biochem, Inc. V. Gen-Probe Inc., 296 F.3d 1316, 63 USPQ2d 1609 (Fed. Cir. 2002). The Enzo court adopted the standard that the written description requirement can be met by "show[ing] that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics ....i.e., complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics. " Id. At 1324, 63 USPQ2d at 1613 (emphasis omitted, bracketed material in original).

Thus, the instant specification may provide an adequate written description of the genus of antibodies, per Lilly by structurally describing a representative number of antibodies that function as claimed or by describing structural features common to the members of the genus, which features constitute a substantial portion of the genus. Alternatively, per Enzo, the specification can show that the claimed invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics.

In this case, the specification does not describe the genus of antibodies in a manner that satisfies either the Lilly or Enzo standards. There are insufficient structural features common to all members of the genus of antibodies. The genus of antibodies encompasses any antibody that competes with the binding of the antibody CM-1 to at least one of HT-29, CACO-2, COLO-320 or COLO-678 cells. Applicants have only identified one antibody, CM-1, comprising the amino acid sequences of SEQ ID NOs: 1 and 3 that binds to the epitope on at least one of HT-29, CACO-2, COLO-320, COLO-206F, or COLO-678 cells. The specification does not characterize the antigen to which the antibodies must bind and thus the common structural features of the claimed genus of antibodies is unknown. This description is not sufficient to describe the unlimited number of antibodies in the claimed genus. For purposes of satisfying the written description requirement, it is not enough merely to disclose a method of making and identifying compounds capable of being used to practice the claimed invention. Applicants have not described the antigen bound by the genus of antibodies sufficiently to demonstrate that they had possession of the claimed genus of antibodies that bound this antigen.

Applicants have also not disclosed sufficiently detailed, relevant identifying characteristics, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics. Applicants are not in possession of the epitope bound by CM-1. The specification only discloses that CM-1 specifically binds to at least one of HT-29, CACO-2, COLO-320, COLO-206F, or COLO-678 cells. As indicated above, Applicants have not characterized the antigen to which the antibodies must bind. Thus, the genus of antibodies is described by its functional characteristics, their ability to compete with CM-1 for binding to at least one of HT-29, CACO-2, COLO-320, COLO-206F, or COLO-678 cells. The specific antigen bound by CM-1 was not been adequately described and thus the structure of the antibodies that bind the unknown antigen has not been sufficiently described. Although the requirement for written description may be met by functional characteristics when these characteristics are coupled with a known or disclosed correlation between function and structure, Applicants have not disclosed sufficient

correlation between the functional characteristics of the genus of antibodies and the structure of these antibodies. Applicants have only described one antibody that binds to at least one of HT-29, CACO-2, COLO-320, COLO-206F, or COLO-678 cells and have not characterized the antigen to which the genus of antibodies must bind other than it is expressed on one of HT-29, CACO-2, COLO-320, COLO-206F, or COLO-678 cells.

The specification does not provide an adequate written description of the genus antibodies of claims 79, 95-101 and 103-124 that is required to practice the claimed invention. Applicants have not described the genus of antibodies sufficiently to show they had possession of the claimed genus.

Applicants argue that the law does not require an actual reduction to practice or disclosure of a specific number of examples with the scope of the claims to satisfy the written description requirement. Applicants further argue that examples are not necessary to support adequacy of a written description and cite *Falkner v Ingles* for the proposition that there is no *per se* rule that an adequate written description of an invention that involves a biological macromolecule must contain a recitation of known structure.

The holding in *Falkner* states that:

> "in this case, accessible literature sources clearly provide, as of the relevant date, genes and their nucleotide sequences, satisfaction of the written description requirement does not require either the recitation or incorporation by reference".

Thus, *Falkner* holds that the requirement for a connection between structure and function so as to satisfy the written description requirement is not absolute and that there are instances when the specification does not have to demonstrate a connection between structure and function.

Applicants' arguments have been considered but are not persuasive. In Falkner, the court found that earlier publications that disclosed the DNA sequences of the virus along with knowledge of the essential regions were sufficient to put the inventor in possession of his invention. In the present case there is no prior knowledge about which amino acids of the antibody, CM-1 were essential so that one of ordinary skill in

the art would know with any certainty which amino acids can be added, deleted or substituted and still maintain the binding specificity of CM-1. Applicants have only disclosed one antibody, CM-1, in the claimed genus of antibodies that specifically binds to an epitope of an antigen expressed by at least one of HT-29, CACO-2, COLO-320 or COLO-678 cells. The function of the genus of antibodies is to specifically bind to an epitope of an antigen expressed by at least one of HT-29, CACO-2, COLO-320 or COLO-678 cells, wherein CM-1 antibody specifically binds to said epitope of the antigen expressed by at least one of HT-29, CACO-2, COLO-320 or COLO-678 cells. The region of the antibody that is likely the most important region in determining binding specificity, the heavy chain CDR3 is also the most variable. Previous publications concerning antibody structure do not adequately describe the claimed genus of claimed antibodies in terms of their specific function for the specific function of the claimed genus of antibodies, that is to specifically bind to an epitope of an antigen expressed by at least one of HT-29, CACO-2, COLO-320 or COLO-678 cells, wherein CM-1 antibody specifically binds to said epitope of the antigen expressed by at least one of HT-29, CACO-2, COLO-320 or COLO-678 cells.

Applicants also cite Enzo Biochem v Gen-Probe referring t the Written Description Guidelines that a claim to an isolated antibody capable of binding to antigen X would comply with the written description requirements . Applicants further argue that under Enzo II antibodies are adequately described solely by function and with any reference to a particular antibody sequence or structure, provided there is disclosure of sufficient relevant identifying characteristics of the antibodies, or where the antigen is fully characterized.

However, in Enzo the court stated that

> "the PTO would find compliance with 112, 1, for a claim to an isolated antibody capable of binding to antigen X, notwithstanding the functional definition of the antibody, in light of the well defined structural characteristic for the five classes of antibody, the functional characteristics of antibody binding, and the fact that the antibody technology is well developed and mature. .

There is a distinction between the claim drawn to an antibody as described in Enzo and the antibody in the present case in that the antigen in Enzo was defined whereas in the present case, as in *In re Alonso*, the antigen is not defined. Furthermore, the present claims are drawn to a genus of antibodies in which amino acids of the one identified antibody species are added, deleted or substituted.

Applicants further argue that the epitope of the present claims is defined in terms of expression by at least one of five well defined human cell lines and binding to CM-1 antibody produced by cell line deposited as DSM ACC 2584, or comprising SEQ ID NOs:1 and 3. Applicants argue that one of skill in the art would know, without having to know more about the identity of the epitope, antibodies and functional fragments with in the scope of the claims. Applicants argue that competition binding is a simple and routine technique known in the art at the time of the invention to verify that a given antibody or functional fragment binds to an antigen expressed by a cell – an antibody or functional fragment that compete for CM-1 binding to antigen expressed by at least one of the specifically recited cell lines would be within the scope of the claims, whereas an antibody that did not compete for CM-1 binding to antigen expressed by at least one of the specifically recited cell lines would not be within the scope of the claims.

Thus, Applicants are indicating that experiments must be performed to determine which antibodies are within the scope of the present claims. The Board in Ex Parte Kubin (561 F.3d 1351 (Fed. Cir. 2009) stated that

> Possession may not be shown by merely describing how to obtain possession of members of the claimed genus or how to identify their common structural features. *See University of Rochester*, 358 F.3d at 927, 69 USPQ2d at 1895.

Applicants have only described one antibody within the scope of their claims and a description of how to obtain possession of other members of the claimed genus. Neither the Applicants, nor the art have specifically identified which amino acids may be added, deleted or substitutes and maintain the specific function of the antibody, that is to specifically binds to an epitope of an antigen expressed by at least one of HT-29, CACO-2, COLO-320 or COLO-678 cells, wherein CM-1 antibody specifically binds to

said epitope of the antigen expressed by at least one of HT-29, CACO-2, COLO-320 or COLO-678 cells. Applicants argue that the general function of antibodies, to bind antigen, and the general structural characteristics of antibodies is sufficient to place Applicants in possession of the genus of antibodies. However, given the specific function of the claimed genus of antibodies and the lack of any information on which amino acids are essential to the specific function of the genus of claimed antibodies one of ordinary skill in the art would not know with sufficient certainty which amino acids may be added, deleted or substituted to maintain the specific function of the claimed genus of antibodies, especially within one of the most critical binding regions of the antibody, the heavy chain CDR3. Applicants have not described sufficiently how the other antibodies in the genus besides the antibody comprising SEQ ID NO:1 and 3 are related to the antibody comprising SEQ ID NO:1 and 3 to demonstrate that they had possession of the genus of antibodies in the present claims.

Applicants argue that the claimed antibodies and functional fragments are described both functionally and structurally. Applicants argue that the claimed antibodies bind to the same epitope as the CM-1 antibody, wherein the CM-1 antibody is defined as either an antibody comprising SEQ ID NOs: 1 and 3 or an antibody produced by the cell line deposited as DSM ACC2584. Applicants further argue that antibodies that bind to the same epitope inherently share sequence homology, such as in CDR3 of heavy chain variable region. Applicants argue that antibodies that bind to the same epitope will be expected to inherently share sequence identity to SEQ ID NO:1 and/or 3. Applicants argue that the claimed genus share a common functional (epitope binding) and structural (sequence identity) relationship with SEQ ID and SEQ ID NO:3.

Applicants also argue that because the knowledge and skill in the art in terms of antibody structure correlating with function was high and the predicted location and sequences of the CDRs and FRs in SEQ ID NOs" 1 and 3 that contribute to antigen binding would be known, eh skilled artisan would also have known residues in SEQ ID NOs:1 and 3 amenable to substitution. Applicants argue that in view of the

understanding of the role of CDRs and FRs in antigen binding at the time of the invention, the skilled artisan would know that an amino acid substitution, such as a conservative substitution, insertion or deletion, for example, outside of a CDR or in the FR region of SEQ ID NOs: 1 and 3 would likely not destroy antigen binding activity. Applicants argue that one skilled in the art could have predicted with a high degree of confidence many substitutions of SEQ ID NOs: 1 and 3 that would not destroy binding activity. Applicants cite Xu and Davis who reported that CDR3 of the heavy chain variable region was the primary determinant which confers antigen recognition and specificity. Xu and Davis also stated that the variability of the CDR3 region has a wide range of variations in both length and shape (page 37, 2nd column). Applicants cite Foote and Winter who indicated that framework residue substitutions are tolerated and improve affinity. Thus, amino acids in the FRS may effect the binding affinity of the antibody as well as the binding specificity. Applicants cite Morea et al who reported that changes in the heavy chain CDR3 amino acids accounted for the diversity of responses against various protein antigens and did not require changes to CDR1 or CDR2 sequences. This is supported further by Moreau et al's statement that the H3 region of immunoglobulins is an important source of antibody variability in length, sequence and conformation. (page 290, 2nd column). Applicants cite Padlin for reporting that particular amino acid residues are more prevalent in CDRs/FRs. Applicants cite Knappik et al for reporting the construction of a fully humanized combinatorial antibody library based upon human consensus FRs and CDRs. Knappik et al further stated that for analysis of VH CDR3s all sequences were grouped together because sequence alignments are not possible in this highly diverse region. (page 81, 1st column). Applicants cite Collet et al who reported that heavy chain variable region sequences could productively pair with a variety of different light chain variable region sequences and maintain antigen binding specificity. However, Collett et al also stated that the degree to which a given heavy chain productively paired with any light chain to bind antigen varied from 43% to 100% and depended strongly on the heavy-chain sequence (Abstract).

The references cited by Applicants indicate the high variability of the CDR3 regions between the different antibodies. This would make it very difficult to discern

without experimentation which amino acids are essential to maintain the binding specificity of the antibody. It is noted that the claims, as presently amended, encompass antibodies with substitutions, insertions and/or deletions within the CDR regions of an antibody comprising SEQ ID NOs: 1 and 3. In addition, as Applicants have noted, Foote and Winter disclose that amino acid substitutions in the framework positions can improve the binding affinity of the antibody. This would also indicate that framework residues would contribute to binding specificity. It is well known in the art that small changes within the antibody structure can significantly affect the specific binding function of the antibody. Even minor changes in the amino acid sequences of the heavy and light variable regions, particularly in the CDRs, may dramatically affect antigen-binding function as evidenced by Rudikoff et al (Proc. Natl. Acad. Sci. USA, 79(6):1979-1983, March 1982, cited previously). Colman P. M. (Research in Immunology, 145:33-36, 1994, cited previously) teaches that even a very conservative substitution may abolish binding or may have very little effect on the binding affinity (see pg. 35, top of left column and pg. 33, right column). While there are some publications, which acknowledge that CDR3 is important, the conformations of other CDRs as well as framework residues influence binding. MacCallum et al (J. Mol. Biol., 262, 732-745, 1996, cited previously) analyzed many different antibodies for interactions with antigen and state that although CDR3 of the heavy and light chain dominate, a number of residues outside the standard CDR definitions make antigen contacts (see page 733, right col.) and non-contacting residues within the CDRs coincide with residues as important in defining canonical backbone conformations (see page 735, left col.).

Applicants argue that CDR3 is the most variable and thus would know that an amino acid substitution, such as a conservative substitution, insertion or deletion, for example, outside of a CDR or in the FR region of SEQ ID NOs: 1 and 3 would likely not destroy antigen binding activity. However, the genus of claimed antibodies include amino acid additions, deletions or substitutions within the heavy chain CDR3 region. Furthermore, the CDR3 region of the heavy chain is a region that one of ordinary skill in the art would want to substitute, add or delete amino acids of the antibody comprising SEQ ID NOs: 1 and 3 to increase the binding affinity of the CM-1 antibody.

In addition, Foote and Winter disclose that amino acid substitutions outside the CDRs can effect the specific function of the antibody. MacCallum et al disclose that amino acids outside the CDR regions affect binding specificity. Thus, without further experimentation to determine which amino acids are essential for an antibody that specifically binds to an epitope of an antigen expressed by at least one of HT-29, CACO-2, COLO-320 or COLO-678 cells, wherein CM-1 antibody specifically binds to said epitope of the antigen expressed by at least one of HT-29, CACO-2, COLO-320 or COLO-678 cells, one of ordinary skill in the art would not know which amino acids may be added, deleted or substituted and maintain the specific function of the claimed genus of antibodies, that is to specifically binds to an epitope of an antigen expressed by at least one of HT-29, CACO-2, COLO-320 or COLO-678 cells, wherein CM-1 antibody specifically binds to said epitope of the antigen expressed by at least one of HT-29, CACO-2, COLO-320 or COLO-678 cells. As stated in the Board in Ex Parte Kubin (561 F.3d 1351 (Fed. Cir. 2009)

> Possession may not be shown by merely describing how to obtain possession of members of the claimed genus or how to identify their common structural features. *See University of Rochester*, 358 F.3d at 927, 69 USPQ2d at 1895.

Applicants argue that the facts of Applicants' claimed antibodies are analogous to the facts in *Invitrogen Corp v Clontech Laboratories*, Inc in which the court held that a single embodiment of a protein (a reverse transcriptase) provided an adequate written description for claims directed t a genus of such proteins since the single disclosed protein embodiment had 1) sufficient correlation between structure and function; and 2) shared significant homology with others. Applicants note that the court held that "the shared written description for the patents-in-issue recites both the DNA and amino acid sequences of a representative embodiment of the claimed RT enzyme. Applicants argue that the claims-in-issue in Invitrogen, which did not recite in the claims a particular amount of sequence homology or identity to the reference sequence, satisfied the written description even though there was only a single disclosed embodiment in the

specification. Applicants further argue that in view of Invitrogen, a single embodiment provides an adequate written description of a genus of proteins where there is sufficient correlation between protein structure and function, and members of the species share significant homology.

Applicants arguments have been considered but are not persuasive. Applicants description of the claimed genus of antibodies is not similar to the genus of reverse transcriptases in *Invitrogen*. The genus of reverse transcriptases is sufficiently defined in *Invitrogen*. The specification in *Invitrogen* discloses test data that the enzyme produced by the listed sequence has the claimed features – DNA polymerase activity without RNase H activity. The court in *Invitrogen* stated that in addition to the sequence recited in the specification, the sequences of the RT genes were known and members of the RT family shared significant homologies from one species of RT to another. The court also stated that the specification cited references providing the known nucleotide sequences of these reverse transcriptase genes.

In the present case, Applicants have not identified any other antibody besides CM-1 in the genus of claimed antibodies and there are no cited references identifying any other antibody that belongs to the claimed genus, an antibody that specifically binds to an epitope of an antigen expressed by at least one of HT-29, CACO-2, COLO-320 or COLO-678 cells, wherein CM-1 antibody specifically binds to said epitope of the antigen expressed by at least one of HT-29, CACO-2, COLO-320 or COLO-678 cells. Furthermore, the exact antigen bound by the claimed genus is unknown other than the antigen is bound by the antibody CM-1 and is expressed on at least one of HT-29, CACO-2, COLO-320, COLO-206F, or COLO-678 cells. The genus of antibodies is defined by its function, binding to the same epitope as CM-1 and binding to at least one of HT-29, CACO-2, COLO-320, COLO-206F, or COLO-678 cells. However, Applicants have not identified which amino acids are essential for the binding of CM-1 to its epitope and therefore do not know which amino acids can be added, deleted or substituted and maintained the binding specificity of CM-1. Furthermore, there are no recited references disclosing which amino acids are essential for the specific function of the CM-1 antibody, to bind to a specific epitope on at least one of HT-29, CACO-2, COLO-

320, COLO-206F, or COLO-678 cells. Thus, unlike for the reverse transcriptase in *Invitrogen*, neither applicants nor the art have identified which amino acids are essential for the specific function of the claimed genus of antibodies.

The present case is more similar to that of Ex Parte Kubin (561 F.3d 1351 (Fed. Cir. 2009) where the court found that the written description of 35 USC 112 was not met, stating that

> Without a correlation between structure and function, the claim does little more than define the claimed invention by function. That is not sufficient to satisfy the written description requirement. *See Eli Lilly*, 119 F.3d at 1568, 43 USPQ2d at 1406 ("definition by function ... does not suffice to define the genus because it is only an indication of what the gene does, rather than what it is").

Neither the specification of the present application nor the prior art references define which amino acids are necessary for the specific function of the claimed genus of antibodies, to specifically bind to an epitope of an antigen expressed by at least one of HT-29, CACO-2, COLO-320 or COLO-678 cells, wherein CM-1 antibody specifically binds to said epitope of the antigen expressed by at least one of HT-29, CACO-2, COLO-320 or COLO-678 cells. Thus Applicants have not demonstrated a correlation between the structure of the claimed genus of antibodies and the specific function of the claimed genus of antibodies.

Applicants argue that the facts in *In re Alonso* are distinguishable from the facts and context underlying the present claims. Applicants argue that the claims in *Alonso* are directed to methods of treating neurofibrosarcomas using antibodies idiotypic to the neurofibrosarcomas. Applicants argue that the antibodies In Alonso were not limited to binding to any particular epitope or even any particular antigen. Applicants also argue that the antibodies in Alonso were not defined by or limited to any structure which is distinct from the claims of the present invention in which the claimed antibodies share a common structure due to the binding of the same epitope and claims 106– 123 specifically recite various amounts of sequence identity to light and/or heavy chain

variable regions. Applicants argue that the claimed antibodies and functional fragments share a common structure.

Applicants, argument have been considered but are not persuasive. In both Alonso and in the present case the genus of antibodies in unknown. In both Alonso and the present case there is only one known species in the genus of antibodies. The structure of the antibodies in the present case, other that the antibody comprising SEQ ID NOs: 1 and 3, is unknown. In response to Applicants argument that the claimed antibodies share a common structure, Applicants have not indicated which of the amino acids of the one known species, the antibody comprising SEQ ID NOs: 1 and 3, may be substituted, deleted or added and maintained the function of the antibody, binding to at least one of HT-29, CACO-2, COLO-320 or COLO-678 cells and competes with the binding of the antibody CM-1. Applicants have indicated that the general structure of antibodies is known and therefore antibody regions having a high degree of variability is known. However, each antibody has its distinct function, binding to its particular epitope. Knowing which amino acid to add, delete or substitute for one antibody would not be indicative of which amino acid may be added, deleted or substituted for another antibody that binds to a different epitope. Knowing the structure of antibodies in general gives one a general framework as to which amino acids may be substituted, deleted or added and bind the same epitope as CM-1 but without further experimentation, the specific amino acid changes that can be made without changing the binding characteristics of the antibody comprising SEQ ID NOs: 1 and 1 are unknown. Furthermore, the genus of antibodies claimed in the present invention are not limited to a specific antibody structure in which the only amino acids that are added, deleted or substituted are within those regions of the antibody in which amino acid changes are most likely to be tolerated. The genus of antibodies claimed in the present invention, include antibodies in which amino acids have been added, deleted or substituted in the CDR3 region of SEQ ID NO:1, the heavy chain variable region of CM-1, the region of the antibody which has a high degree of variability. Changes within the CDR3 region of the CM-1 antibody would be desirable to increase the binding affinity of the antibody.

As stated in the Board in Ex Parte Kubin (561 F.3d 1351 (Fed. Cir. 2009)

> Possession may not be shown by merely describing how to obtain possession of members of the claimed genus or how to identify their common structural features. *See University of Rochester*, 358 F.3d at 927, 69 USPQ2d at 1895.

Without further experimentation, Applicants do not know the structure of the antibodies in the genus of claimed antibodies other than the antibody comprising SEQ ID NOs: 1 and 3. Furthermore, the exact size of the genus of claimed antibodies is unknown since the number of amino acid changes that can be made and still maintained the binding characteristics of the antibody, CM-1, is unknown. In addition, Applicants have not demonstrated a correlation between the structure of the claimed genus of antibodies and the specific function of the claimed genus of antibodies.

Summary

Claims 79, 95-101 and 104-124 stand rejected.

Claim 102 and 103 are allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mark Halvorson, PhD whose telephone number is (571) 272-6539. The examiner can normally be reached on Monday through Friday from

8:30am to 5 pm. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms, can be reached at (571) 272-0832. The fax phone number for this Art Unit is (571) 273-8300.

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